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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/784,028	02/21/2004	Philip Hallinger Bonner	989-002	1705
37468	7590	10/10/2006	EXAMINER	
STOCKWELL & ASSOCIATES, PSC 861 CORPORATE DRIVE, SUITE 201 LEXINGTON, KY 40503			FORD, VANESSA L	
			ART UNIT	PAPER NUMBER
			1645	

DATE MAILED: 10/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/784,028	<b>Applicant(s)</b> BONNER ET AL.	
	<b>Examiner</b> Vanessa L. Ford	<b>Art Unit</b> 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 2/21/04.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 February 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>5/14/04</u> . | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Specification***

1. The use of trademarks has been noted in this application. See for example, page 22. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Applicant is asked to review the specification for various trademarks and appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

### ***Written Description***

2. Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph as containing subject matter which lacks written description in the specification in such a way as to enable one skilled in the art to which it pertains or with which it is most nearly connected to make and/or use the invention.

The claims are drawn to a method of extending the duration of the therapeutic effect of botulinum toxin in an animal comprising the steps of administering a botulinum

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toxin to treat a condition or disorder and administering an inhibitor of the protein tyrosine kinase pathway in an amount sufficient to extend the duration of the effect of botulinum toxin therapy.

The claims broadly encompasses prolonging the period of response to a therapeutic treatment with botulinum toxin. The instant specification discloses in the experimental examples that genistein prolongs the paralytic effects of botulinum toxin on orbicularis oculi muscles and foreleg flexor muscles. However, the instant specification fails to adequately describe the claimed method using a population of subjects that have a condition or disorder (e.g. condition or disorder involving the skeletal neuromuscular system or autonomic nervous system). The instant specification incorporates by reference numbers publications that discloses conditions or disorders that are treatable by administration of botulinum toxin. However, the instant specification fails to provide a method that treats a subject that has a skeletal neuromuscular system or autonomic nervous system condition or disorder by administering botulinum toxin and a tyrosine kinase inhibitor such as genistein. To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as

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to reasonably convey to the skilled artisan that Applicant has possession the claimed invention.

It should be remember that MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed. See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991).

One skilled in the art would not recognize from the claimed disclosure that Applicant was in possession of a method of extending the duration of the therapeutic effect of botulinum toxin in an animal by administering botulinum toxin to treat a condition or disorder and administering an inhibitor of the protein kinase pathway at the time of filing.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-20 is rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites "an amount sufficient to ...". It is unclear as to what the applicant is referring? Correction is required.

4. Claims 1-20 is rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites the active step of administering the botulinum toxin and the protein tyrosine kinase, however, it is unclear as to what these compounds are being administered to. Does Applicant intend that the claimed method is performed *in vitro*, *in vivo* or *ex vivo*? Correction/clarification is required.

The Examiner is broadly interpreting the claimed method to encompass "*in vitro* assays" based on the rejection under 35 U.S.C. 112, second paragraph rejection set forth above. (See paragraph 4).

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-20 are rejected under 35 U.S.C. 102(a) as anticipated by Griffin et al (*SouthEast Nerve Net, 2002*)(*Abstract*).

The claims are drawn to a method of extending the duration of the therapeutic effect of botulinum toxin in an animal comprising the steps of administering a botulinum toxin to treat a condition or disorder and administering an inhibitor of the protein tyrosine kinase pathway in an amount sufficient to extend the duration of the effect of botulinum toxin therapy.

Griffin et al teach a method of administering botulinum toxin and genistein to chick skeletal muscles as well as chick ciliary ganglion motor neurons (see the *Abstract*). Griffin et al teach that botulinum toxin paralyzes skeletal muscle by blocking fusion synaptic vesicles with the presynaptic membrane at neuromuscular junctions (see the *Abstract*). Griffin et al teach that in addition to blocking vesicle fusion, botulinum toxin A causes axons to branch by an unknown mechanism (see the *Abstract*). Griffin et al teach that axon branching induced by botulinum toxin A was significantly reduced in both genistein and 17 $\beta$ -estradiol-treated cultures, suggesting the

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the genistein and estrogen may be acting through a similar mechanism that inhibits branching (see the Abstract). Griffin et al teach genistein reduces botulinum toxin induced sprouting, thereby prolonging the action of the botulinum toxin. Thus, the claim limitation "extending the duration of the therapeutic effect of botulinum toxin" is inherently taught by the prior art. Therefore, Griffin et al anticipate the claimed invention.

6. Claims 1-20 are rejected under 35 U.S.C. 102(b) as anticipated by Radmanesh et al (*Society for Neuroscience Abstracts*, 200, Vol. 26, No. 1-2)(Abstract).

The claims are drawn to a method of extending the duration of the therapeutic effect of botulinum toxin in an animal comprising the steps of administering a botulinum toxin to treat a condition or disorder and administering an inhibitor of the protein tyrosine kinase pathway in an amount sufficient to extend the duration of the effect of botulinum toxin therapy.

Radmanesh et al teach a method of administering botulinum toxin and genistein to chick skeletal muscles as well as chick ciliary ganglion motor neurons (see the Abstract). Radmanesh et al teach the botulinum toxin A paralyzes skeletal muscle by blocking fusion of synaptic vesicles with presynaptic membrane at neuromuscular junctions (see the Abstract). Radmanesh et al teach that botulinum toxin A is used clinically for the relief of symptoms of certain spasmodic muscle contraction disorders, but unwanted contractions eventually return because of new synapses formed by branches sprouted from the original axons (see the Abstract). Radmanesh et al teach



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that axon sprouting induced by toxin both motor and sensory neurons is significantly reduced by protein tyrosine kinase inhibitors, especially genistein. Radmanesh et al teach that branching arborization of non-toxin-treated motor and sensory neurons is similarly reduced by inhibitor, suggesting that the mechanisms underlying toxin-induced branching may be similar to those of normal developmental or regenerative branching (see the Abstract). Radmanesh et al teach genistein reduces botulinum toxin induced sprouting to a level that is similar to those of normal developmental, therefore, the action of the toxin is prolonged. Thus, the claim limitation "extending the duration of the therapeutic effect of botulinum toxin" is inherently taught by the prior art. Therefore, Radmanesh et al anticipate the claimed invention.

### ***Status of Claims***

7. No claims allowed.

**Conclusion**

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vanessa L. Ford whose telephone number is (571) 272-0857. The examiner can normally be reached on 9 am- 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Albert Navarro can be reached on (571) 272-0861. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



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September 29, 2006



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